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A model to assess the utility of risk-based breast cancer screening algorithms

Emma C. Atakpa, Jack Cuzick, Stephen W. Duffy, D. Gareth Evans, Sacha J. Howell, Adam R. Brentnall

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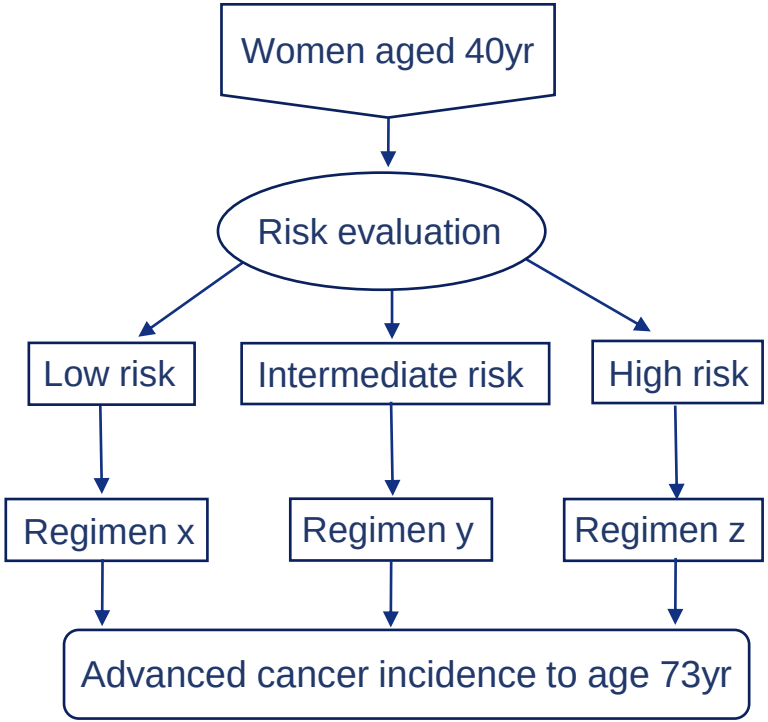
Background

- In the UK, NICE guidelines (CG164) recommend annual mammography screening from 40yr in women at moderate/high-risk of breast cancer based on family history or high-risk genes
- For most women, risk assessment isn't routinely done – they are screened using an age-based "one-size-fits-all" approach (triennial screening from 50yr)
- We could improve efficacy by personalising screening based on a comprehensive risk assessment

Photo by National Cancer Institute on Unsplash

Aim: Evaluate different risk-based screening strategies



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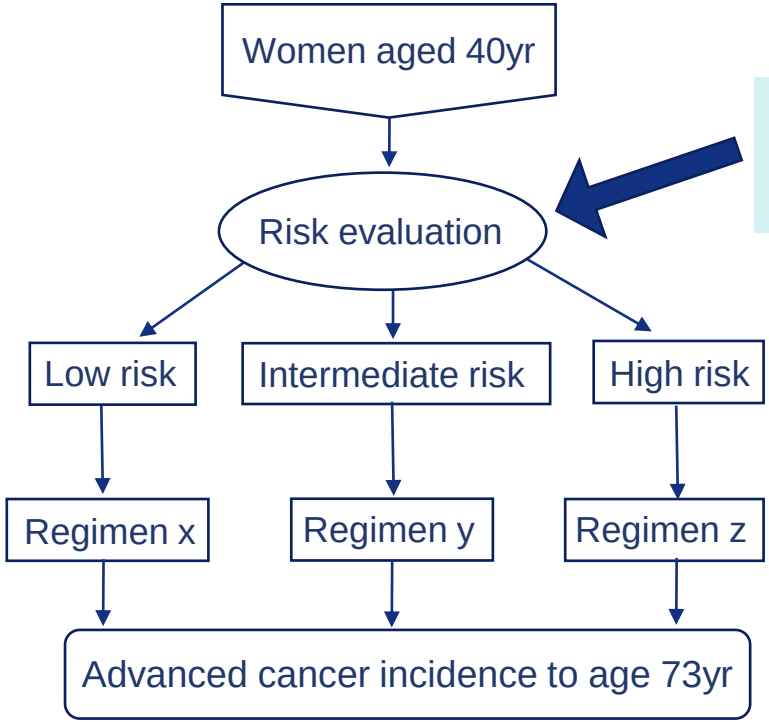

Tyrer-Cuzick 10yr risk (v8 including SNPs & breast density)

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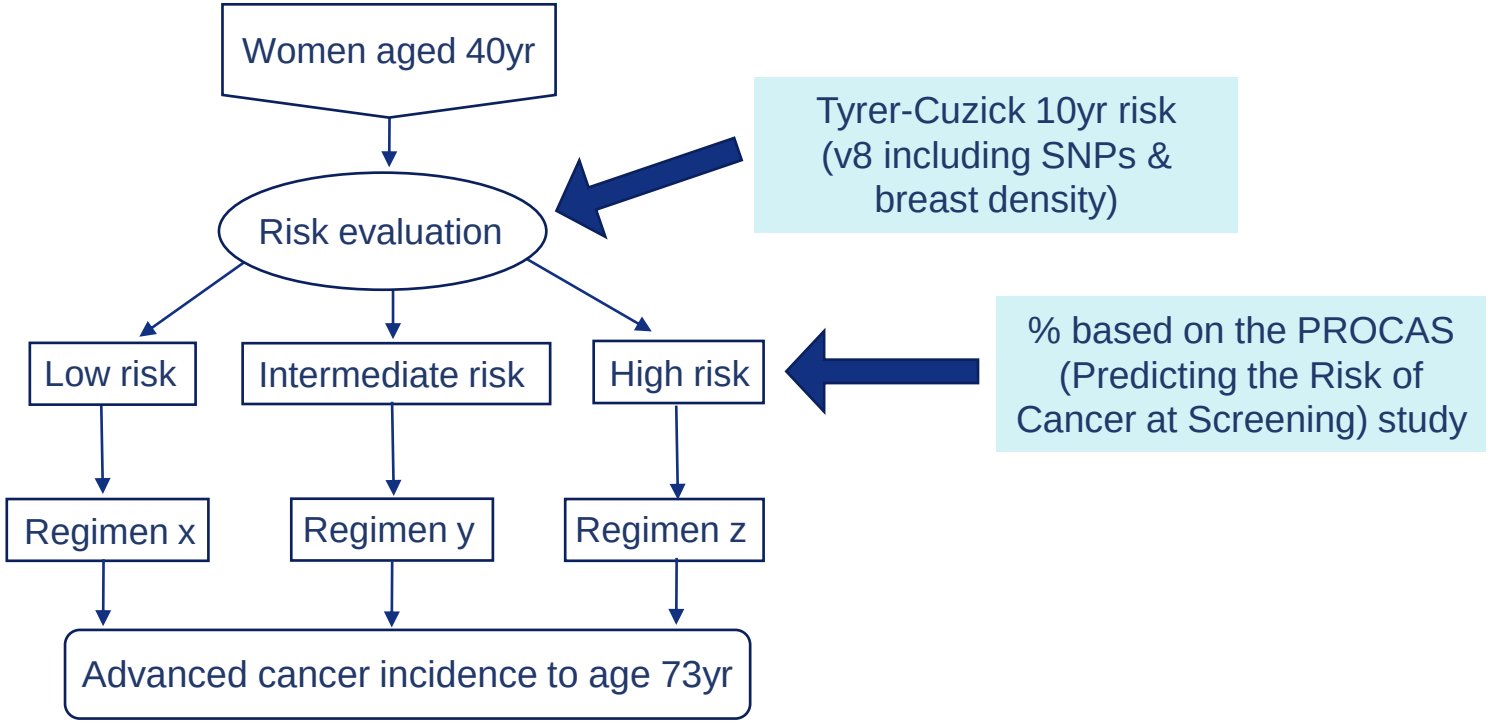

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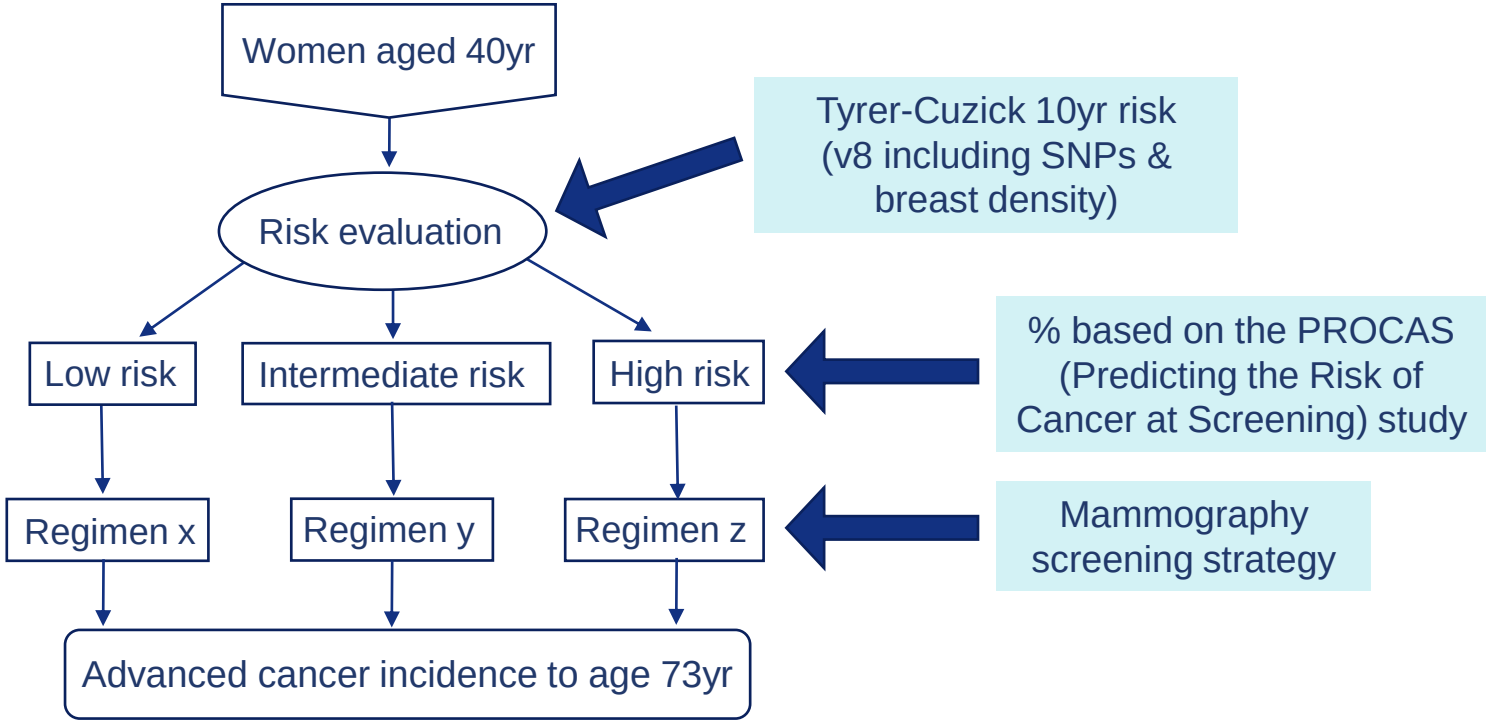

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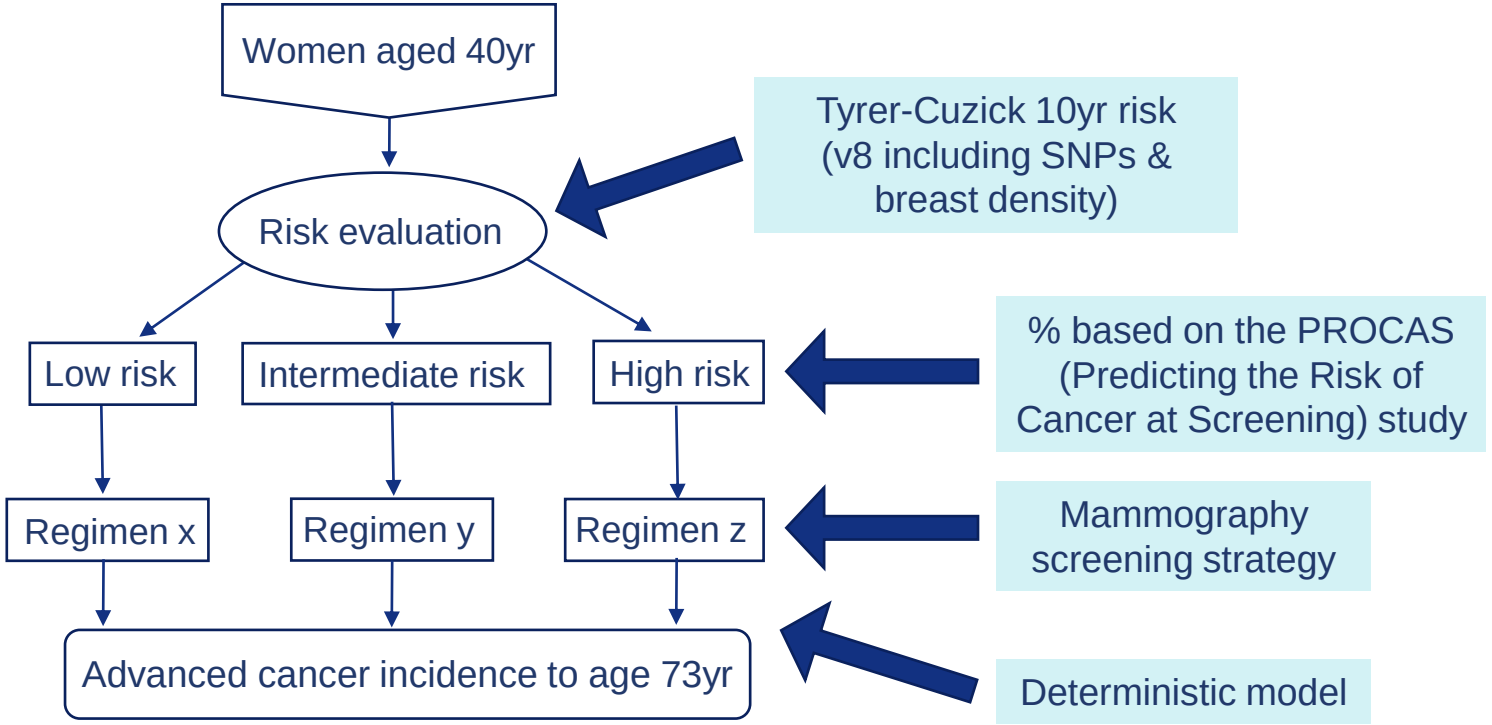

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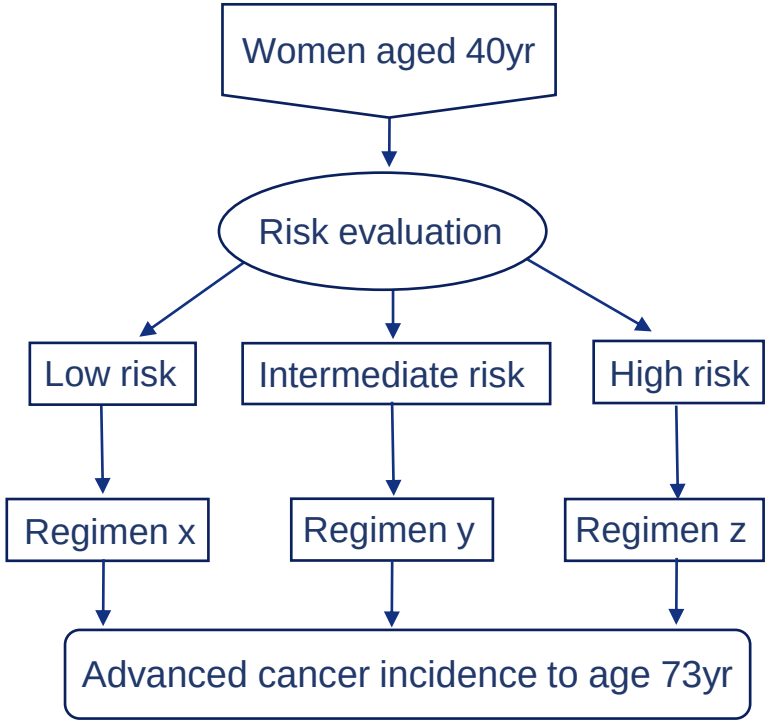
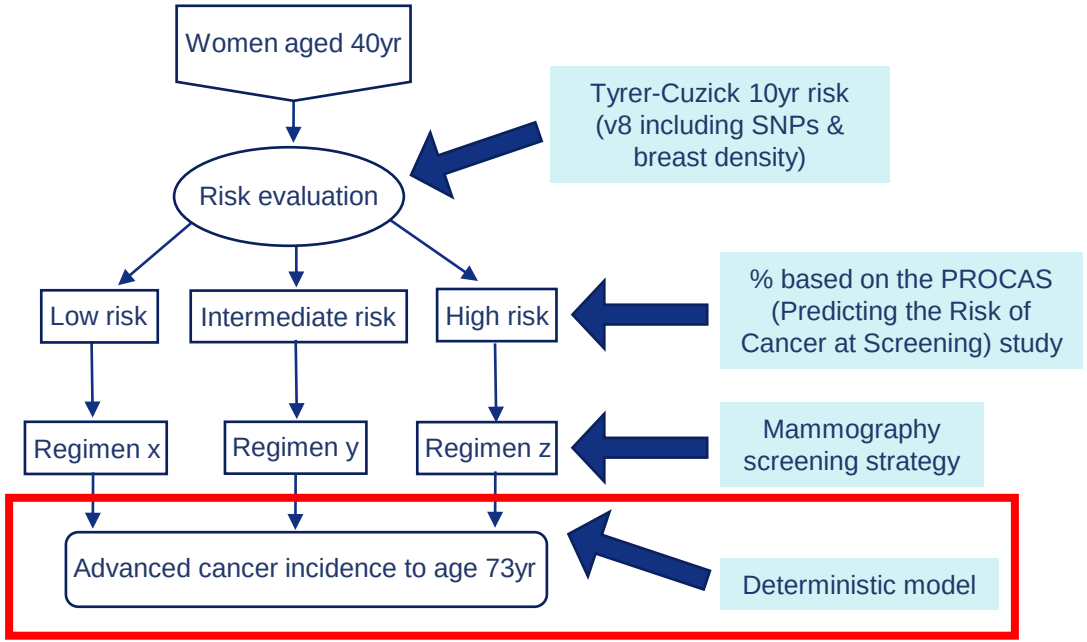


Pros: parsimonious model, easy to interrogate and understand, adaptable to other risk models & settings

Cons: Not as sophisticated as other models (e.g. CISNET), doesn't consider supplemental screening

Model Development



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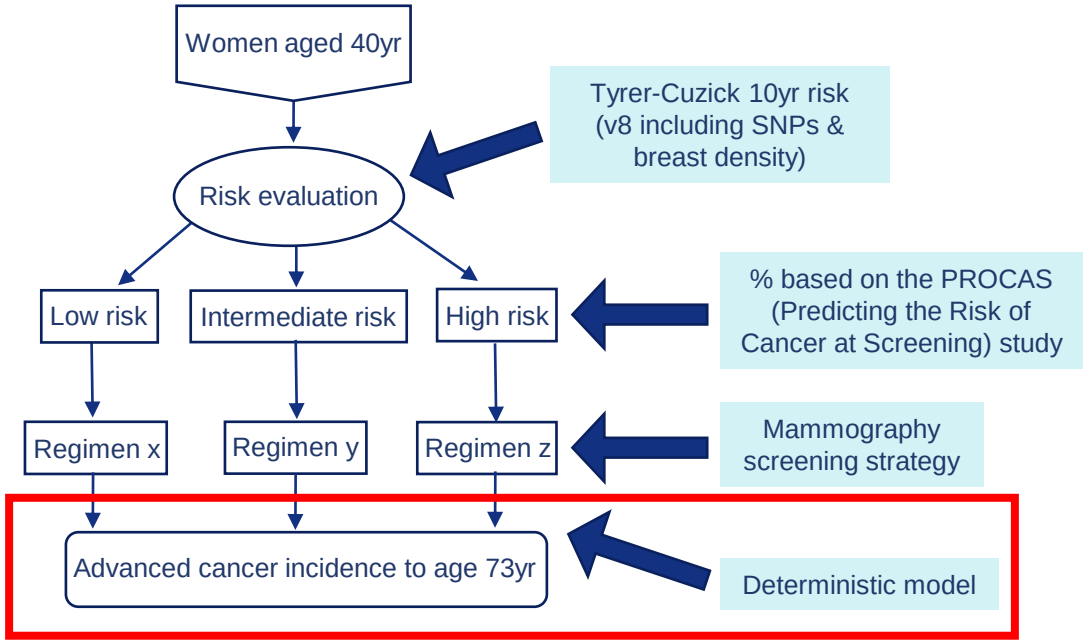

- Estimated proportion of screen-detected cancers and proportion of interval cancers for screening intervals (every 1/2/3/4/5yr)

Model Development

- Proportion of screen-detected cancers (P) for given screening intervals (r):

$$P = \frac{S(1-e^{-\lambda r})}{\lambda r(1-(1-S)e^{-\lambda r})}$$ [1] ⟶ Proportion of interval cancers = $1 - P$

[1] Launoy G, et al. Dépistage des cancers: sensibilité du test et de la procedure de dépistage. Revue d'Épidemiologie et de Santé Publique 1998; 46: 420-6

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S (sensitivity of mammography) = 0.92

λ (annual transition rate asymptomatic to symptomatic) = 0.25 [2]

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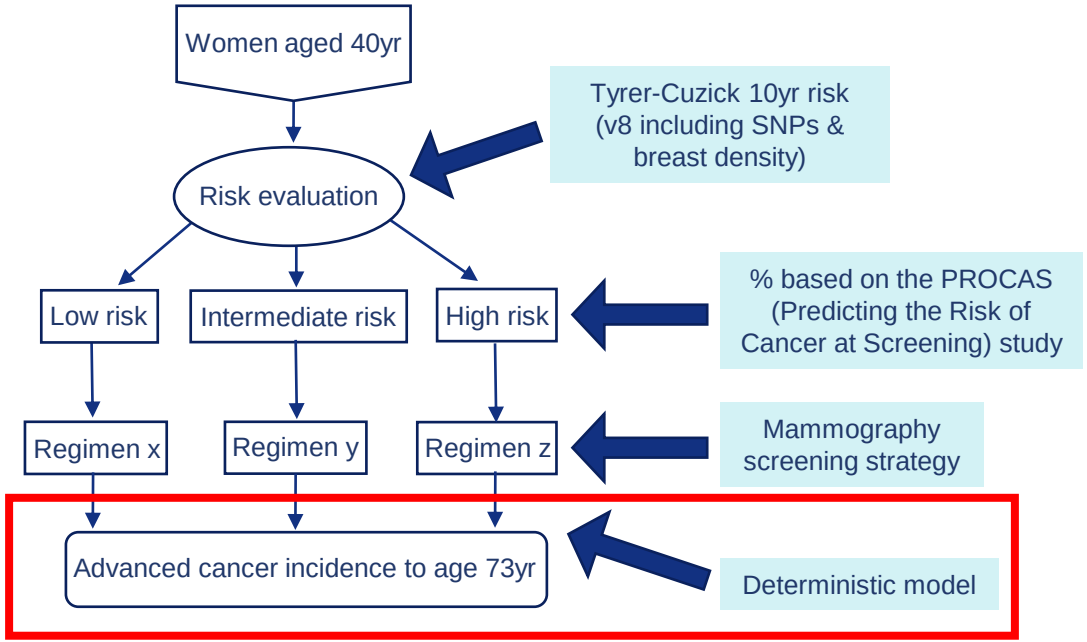
Model Development



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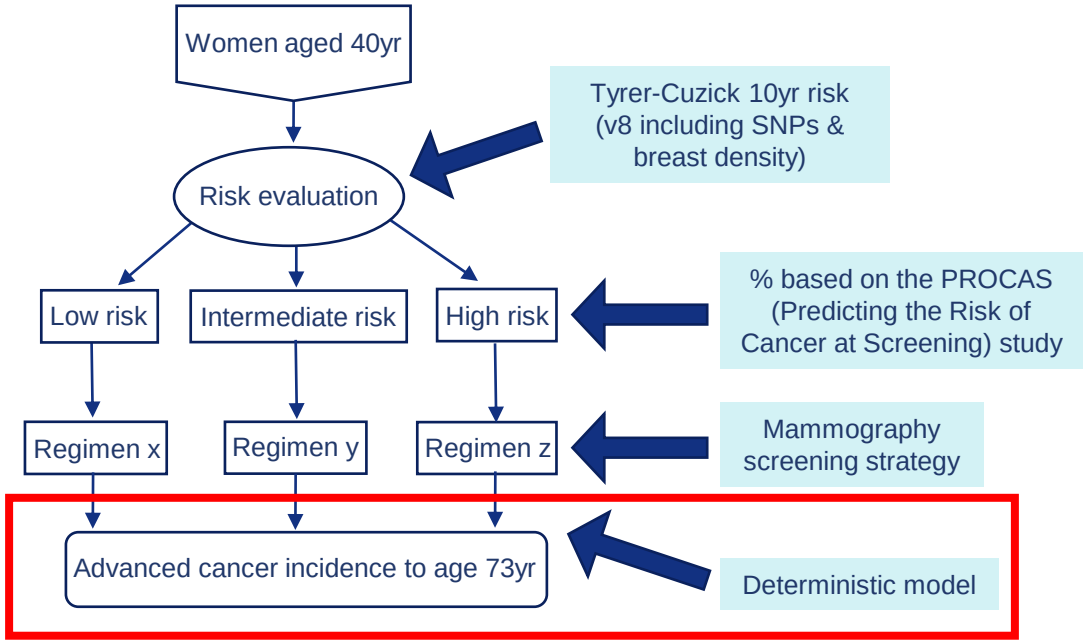

- Estimated proportion of screen-detected cancers and proportion of interval cancers for screening intervals (every 1/2/3/4/5yr)
- Estimated proportion of screen-detected cancers that are node+ and proportion of interval cancers that are node+

Model Development

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Model Development

- Proportion of screen-detected cancers (P) for given screening intervals (r):

$$P = \frac{S(1-e^{-\lambda r})}{\lambda r(1-(1-S)e^{-\lambda r})} \quad [1] \longrightarrow \text{Proportion of interval cancers} = 1 - P$$

S (sensitivity of mammography) = 0.92

λ (annual transition rate asymptomatic to symptomatic) = 0.25 [2]

- Proportion of screen-detected cancers which are node+ = 22%
- Proportion of interval cancers which are node+ = 53% [3]

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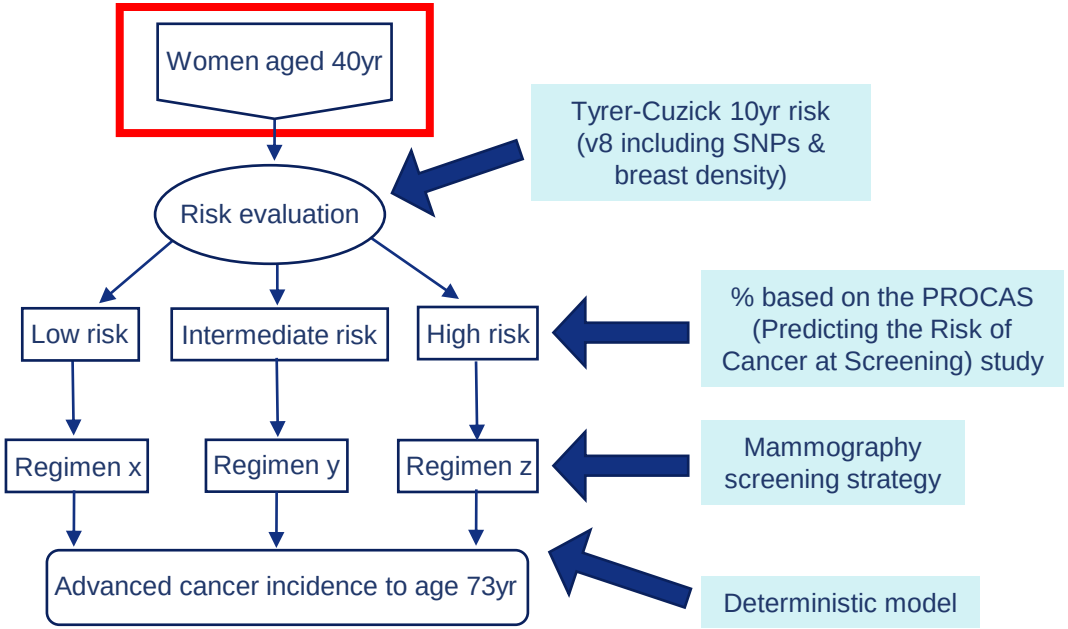
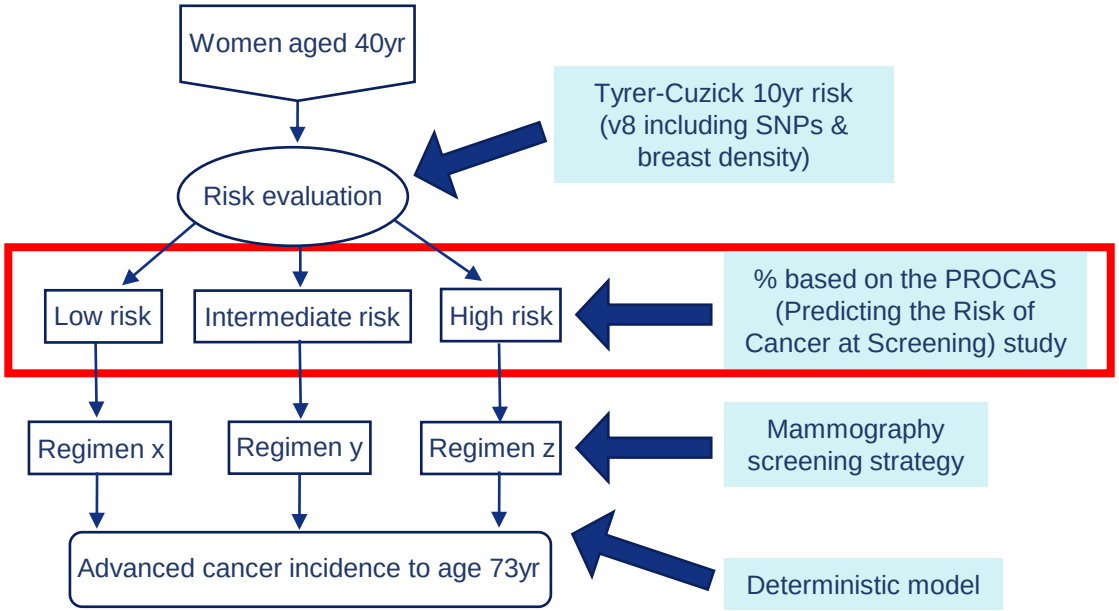
[2] Tabar L, et al. The Swedish Two-county trial twenty years later: updated mortality results and new insights from long term follow-up. Radiol Clin Nth Amer 2000; 38: 625–51
[3] NHS Breast Screening Programme (England, 2015-18, women aged ≥47yr)

Simulated women



Hypothetical cohort of 3.45M women

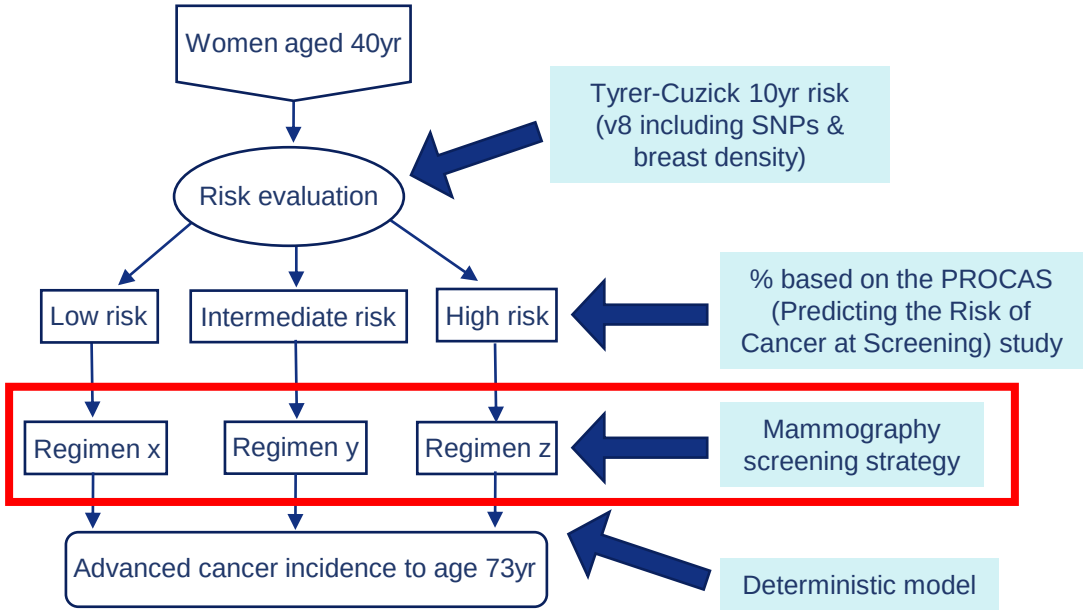
Simulated women



Hypothetical cohort of 3.45M women

1M women identified as either:
High-risk (>8% absolute risk; n=241,379)
or
Low-risk (<1.4% absolute risk; n=758,621)

Regimens


Women aged 40yr
Tyrer-Cuzick 10yr risk (v8 including SNPs & breast density)
Risk evaluation
Low risk
Intermediate risk
High risk
% based on the PROCAS (Predicting the Risk of Cancer at Screening) study
Regimen x
Regimen y
Regimen z
Mammography screening strategy
Advanced cancer incidence to age 73yr
Deterministic model

Scenarios

1: Risk-based screening interval 50-70yr

2: Risk-based starting age 45-56yr

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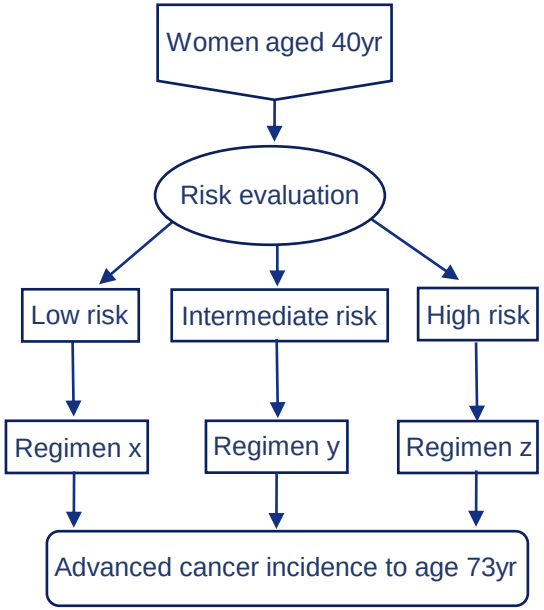
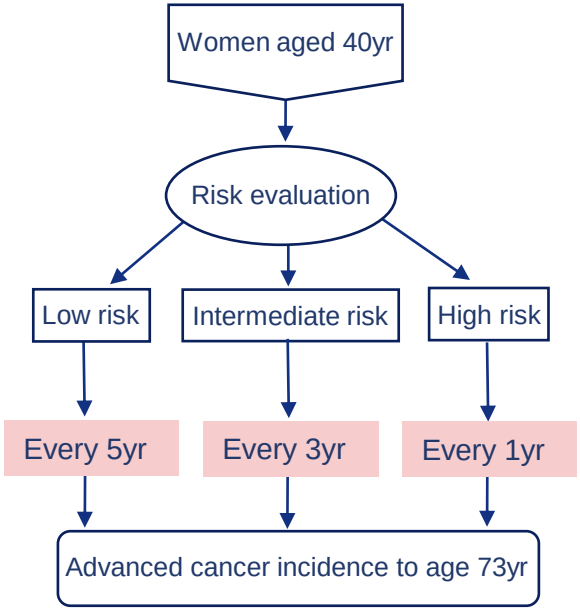
Scenario 1: Changing screening interval based on risk



Scenario 1: Changing screening interval based on risk

Start screening at 50yr



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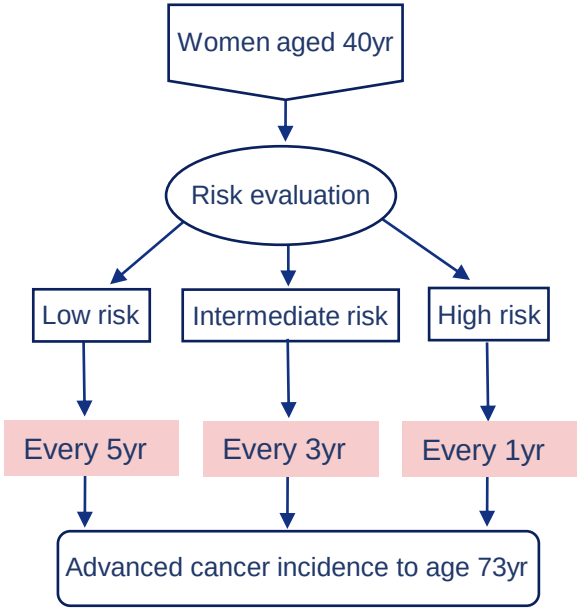
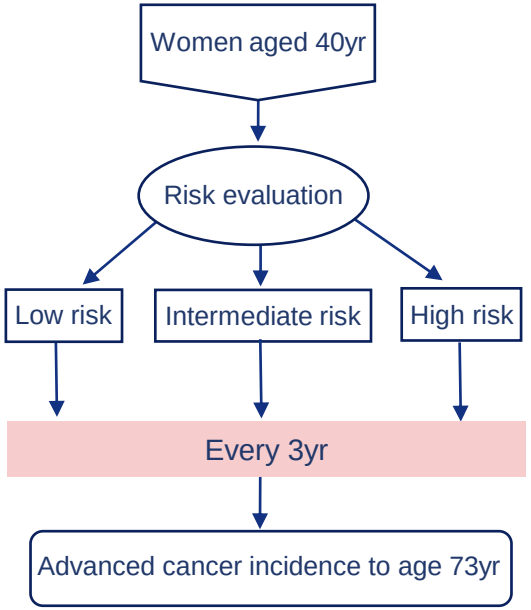


V.S.



(Same screening as NHSBSP)

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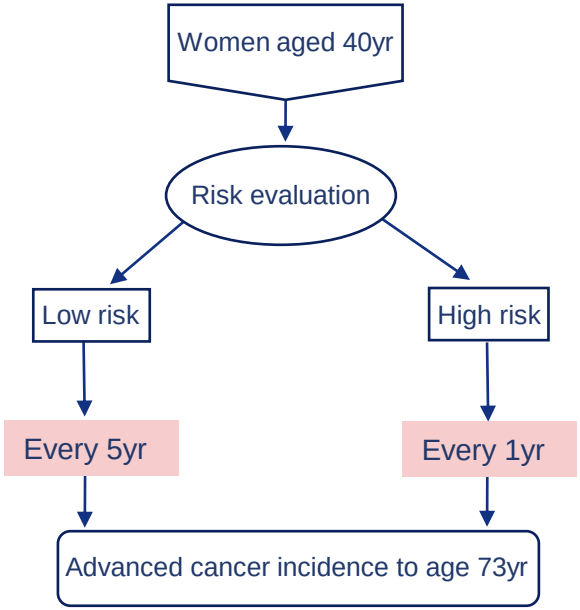

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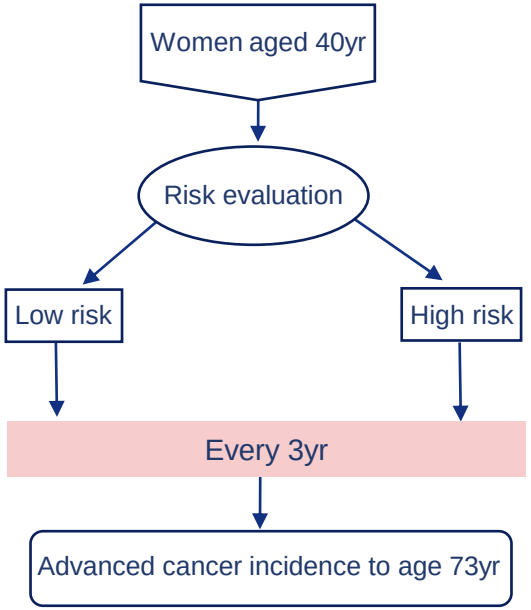

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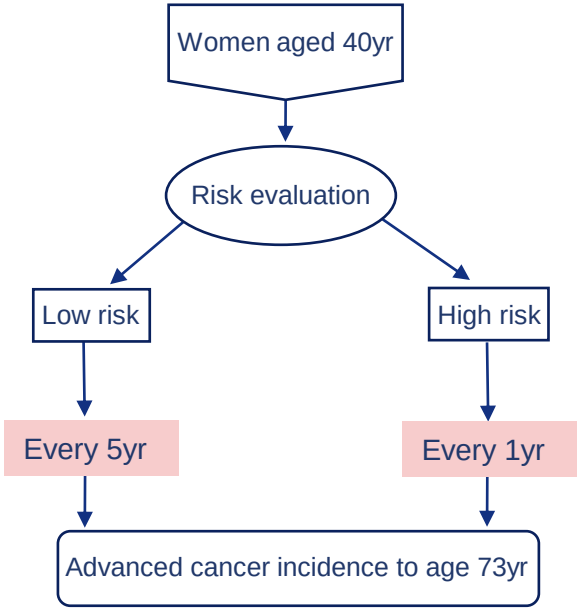

+ How many screens?

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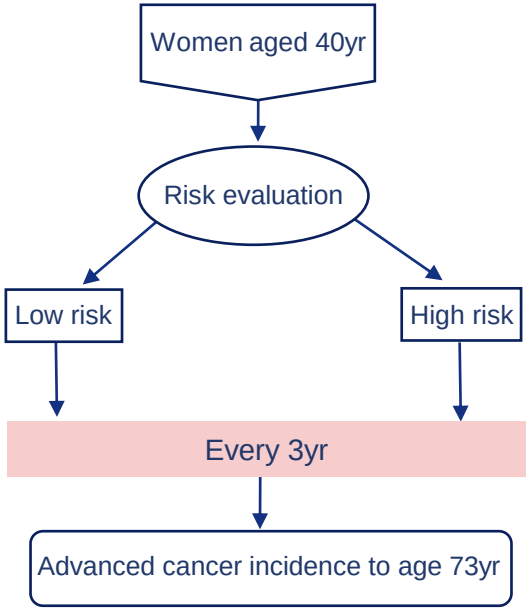

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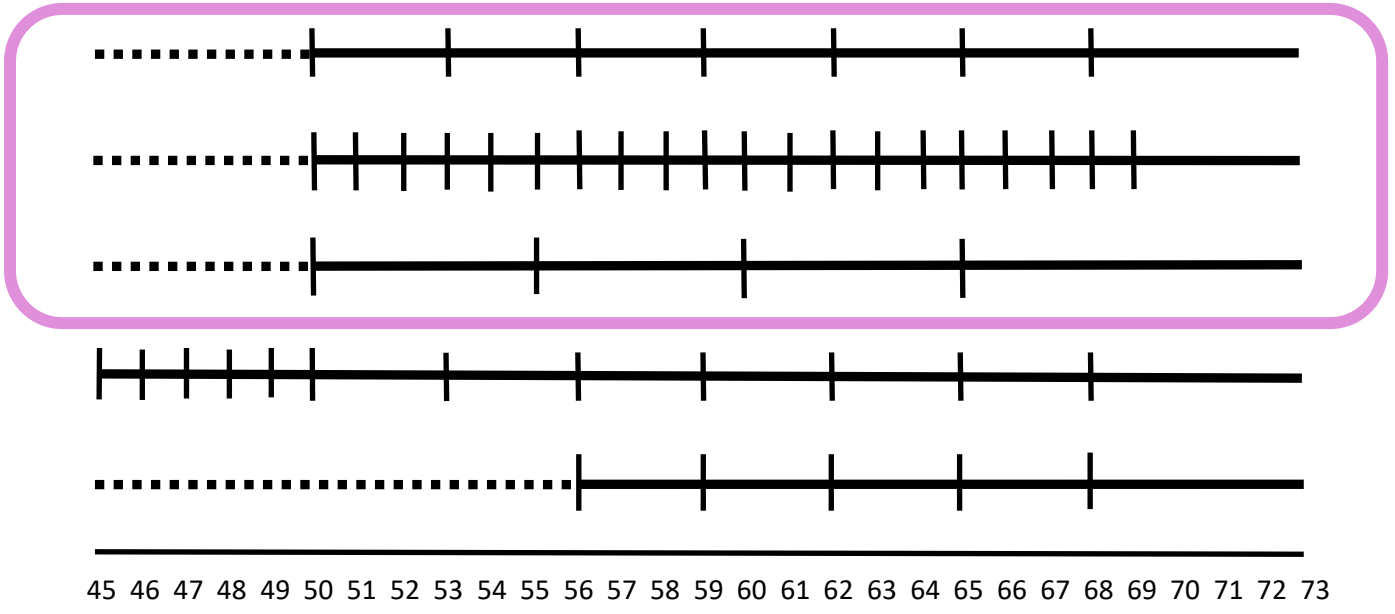
45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73
Age (years)
Key:
Period of screening
Period of no screening
Screening event

Scenario 1: Changing screening interval based on risk

Assess trade-off between:

Decreased no. of node+ with high-risk regimen

and

Increased no. of node+ with low-risk regimen

Assess trade-off between:

Increased no. of screens with high-risk regimen

and

Decreased no. of screens with low-risk regimen

Results: Changing screening interval based on risk

High-risk (n=241,379; 24%)

	Node+	Screens
Usual screening	11,640	1,689,655
Risk-based screening	9,446	4,827,586
	Δ No. of node+	Δ No. of screens
Risk-based vs Usual screening	-2,194	+3,137,931

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Low-risk (n=758,621; 76%)

	Node+	Screens
Usual screening	6,984	5,310,345
Risk-based screening	7,894	3,034,483
	Δ No. of node+	Δ No. of screens
Risk-based vs Usual screening	+910	-2,275,862

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TRADE-OFF (High-risk vs Low-risk)

	Δ No. of node+	Δ No. of screens
Risk-based vs Usual screening	**-1,283 (-1.4%)**	**+862,069 (+3.6%)**

Scenarios

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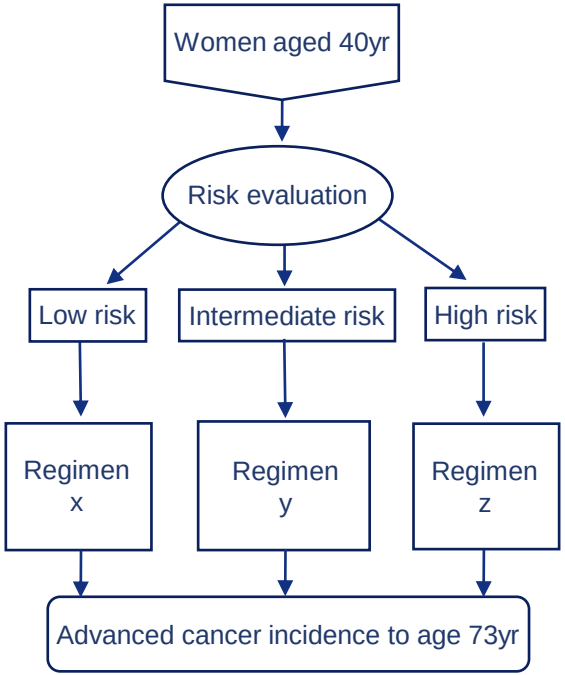
Scenario 2: Changing screening starting age based on risk



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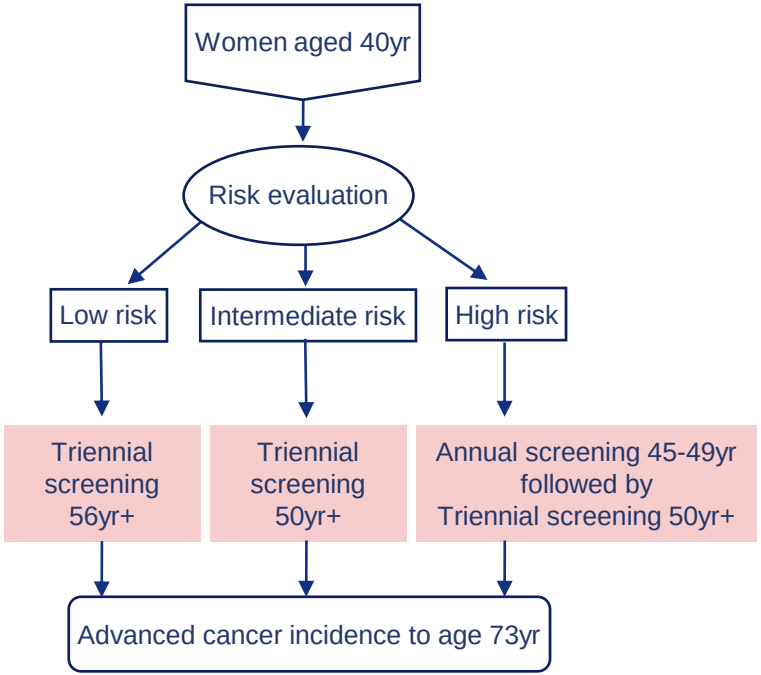

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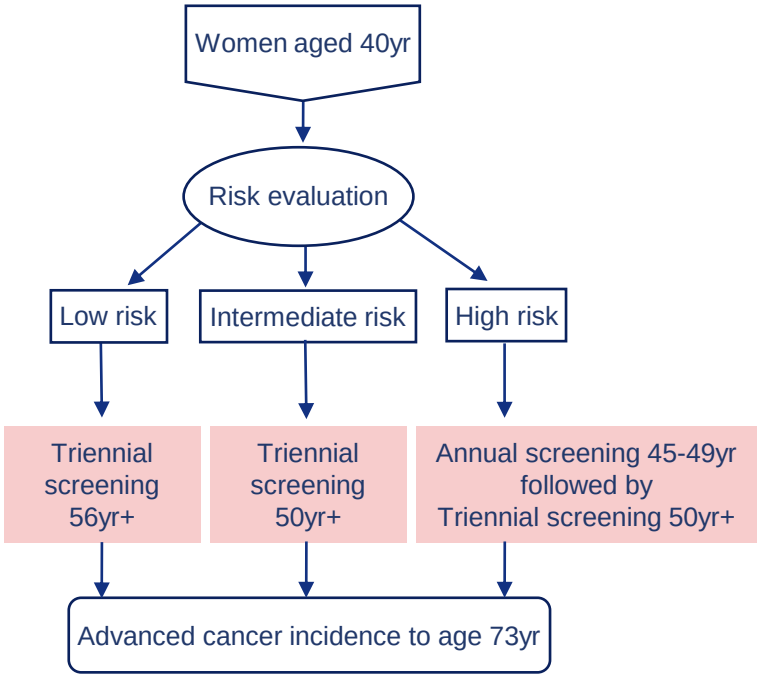

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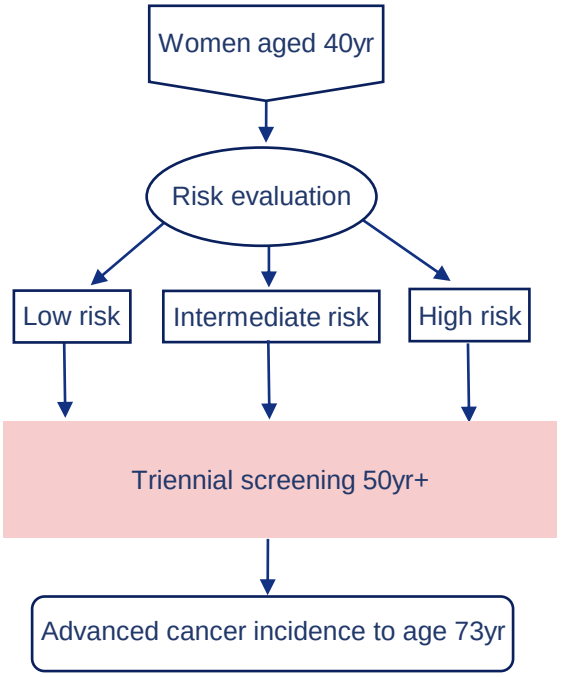

(Same screening as NHSBSP)

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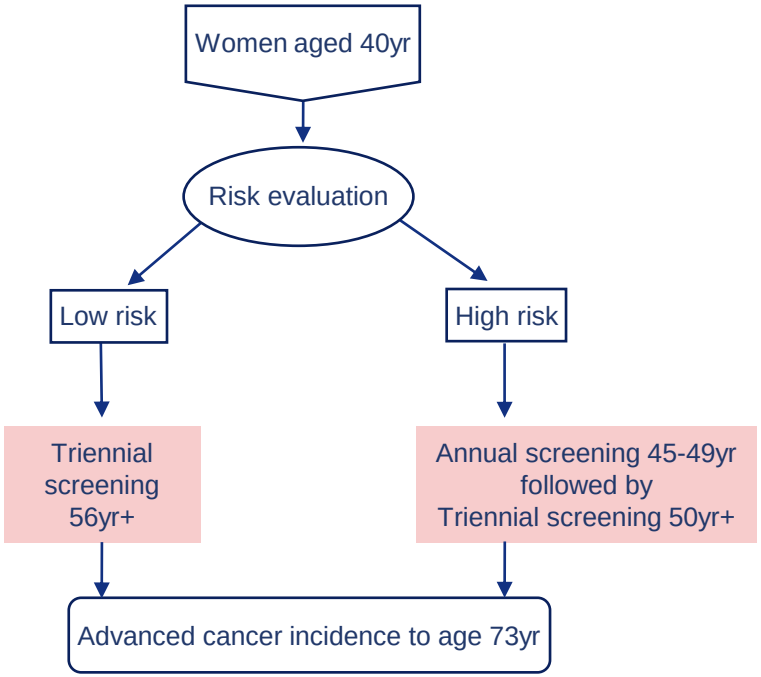

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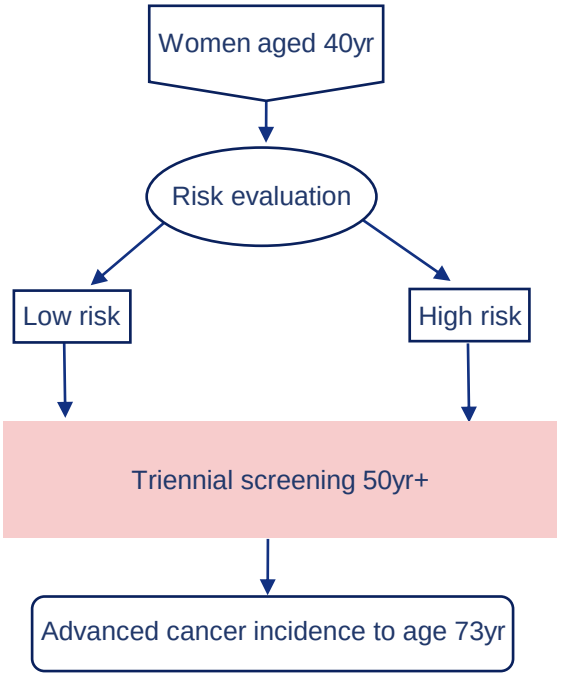

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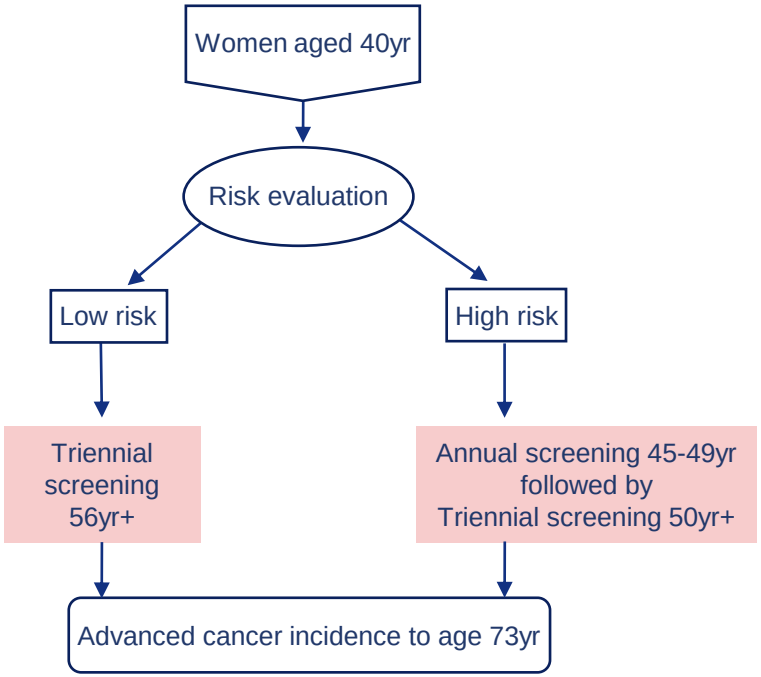

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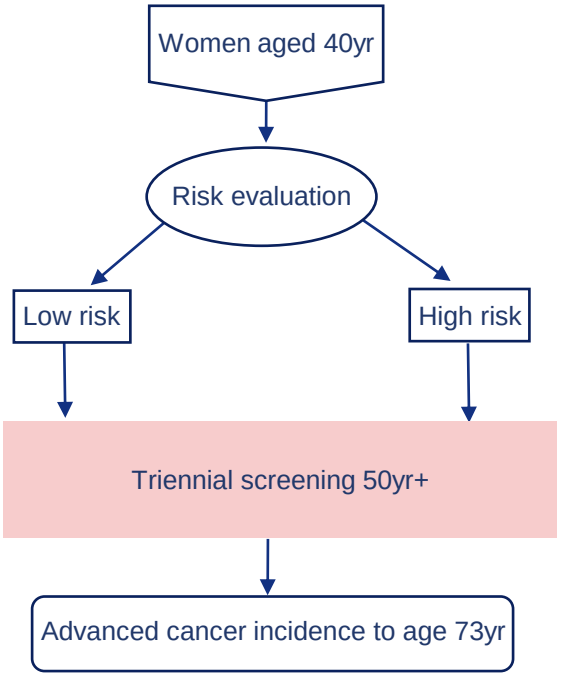

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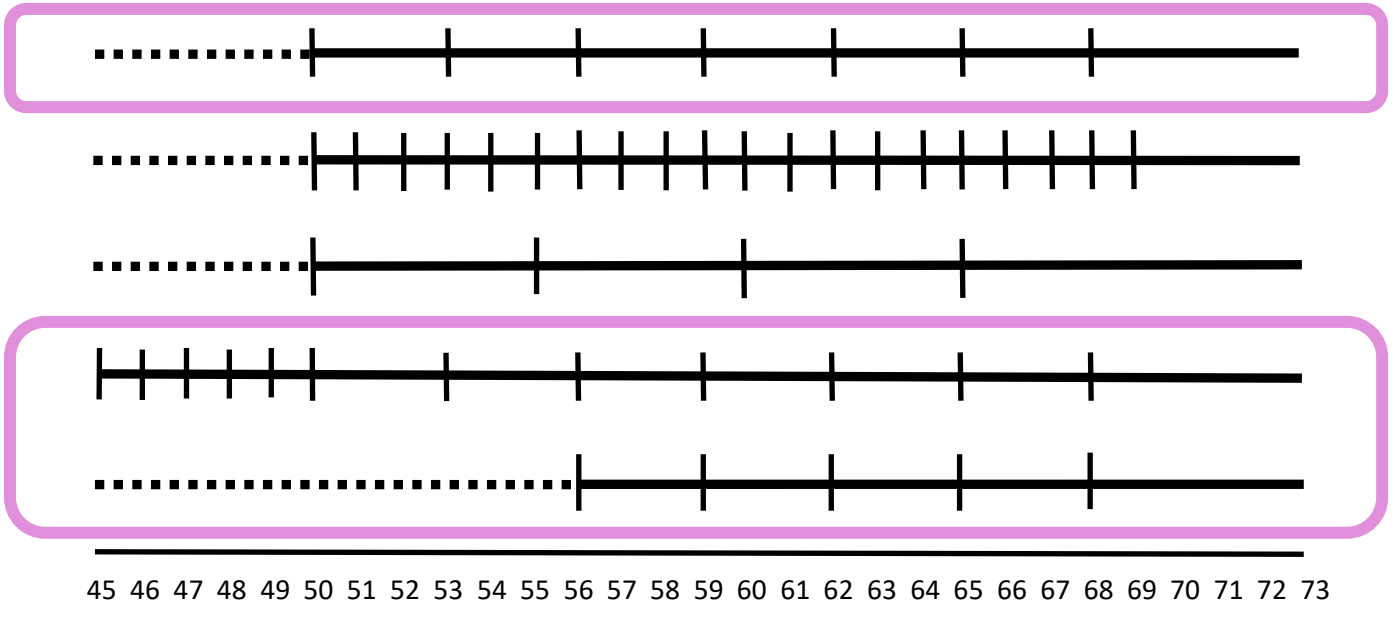
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Age (years)
Key:
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Scenario 2: Changing screening starting age based on risk

Assess trade-off between:

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and

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Results: Changing screening starting age based on risk

High-risk (n=241,379; 24%)

	Node+	Screens
Usual screening	2,224	0
Risk-based screening	1,349	1,206,897
	Δ No. of node+	Δ No. of screens
Risk-based vs Usual screening	-875	+1,206,897

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Low-risk (n=758,621; 76%)

	Node+	Screens
Usual screening	1,596	1,517,241
Risk-based screening	2,135	0
	Δ No. of node+	Δ No. of screens
Risk-based vs Usual screening	+539	-1,517,241

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TRADE-OFF (High-risk vs Low-risk)

	Δ No. of node+	Δ No. of screens
Risk-based vs Usual screening	**-336 (-0.4%)**	**-310,345 (-1.3%)**

Sensitivity analyses

- Exclude breast density (no baseline mammogram for risk assessment)
- Vary model parameter estimates & risk estimates by ±10%
- Vary model parameter estimates by ±10% (45-50yr)

Sensitivity analyses

Scenario 1 (Risk-based screening interval):
Δ No. of node+: between -1.6% and -1.1%
Δ No. of screens: between +1.7% and +3.6%

Scenario 2 (Risk-based starting age):
Δ No. of node+: between -0.4% and -0.3%
Δ No. of screens: between -1.5% and -1.3%

Conclusion

Changing the starting age of screening based on long-term risk is likely to be more effective per screen required at reducing the incidence of advanced breast cancer than changing the screening interval based on long-term risk

Thank you


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